INTRODUCTION

In order to promote the appropriate use of new or emerging endoscopic technologies, the ASGE Technology Committee has developed a series of status evaluation papers. By this process relevant information about these technologies may be presented to practicing physicians for the education and care of their patients. In many cases, data from randomized controlled trials is lacking and only preliminary clinical studies are available. Practitioners should continue to monitor the medical literature for subsequent data about the efficacy, safety and socioeconomic aspects of the technologies.

BACKGROUND

Propofol, or 2-6 diisopropylphenol (AstraZeneca, Wilmington, DL; Baxter Pharmaceutical Products, Inc., New Providence, NJ) is an ultrashort acting sedative hypnotic agent that has received increased attention for use during endoscopy.\(^1\)-\(^7\) The distinctive sedative properties, pharmacokinetics, and pharmacodynamics form the basis of this report.

PHARMACOLOGIC PROPERTIES

Propofol is an alkyl phenol derivative that possesses sedative, amnestic, and hypnotic properties but provides minimal analgesia.\(^8\),\(^9\) The drug is lipophilic and is prepared as an oil/water emulsion consisting of 1% propofol, 10% soybean oil, 2.25% glycerol, and 1.2% egg lecithin.\(^10\),\(^11\) Propofol is contraindicated in patients with hypersensitivity to egg or soybean. In addition, a generic formulation contains sodium metabisulfite and is contraindicated in patients with sulfite allergies.\(^12\)

Propofol has a rapid onset and a short duration of action. Hypnosis is induced within 30-60 seconds of intravenous administration, essentially the time of one arm-brain circulatory pass.\(^8\),\(^9\) The half-life of propofol is 1.8-4.1 minutes. After cessation of infusion, blood concentrations rapidly decline due to rapid tissue distribution and high metabolic clearance.\(^11\) Clinically this accounts for rapid recovery within 10-30 minutes in most patients after discontinuation of the drug.\(^9\)

Propofol is 98% plasma-protein bound, and is metabolized primarily in the liver. Propofol potentiates the effects of benzodiazepines, barbiturates, and opioids.\(^9\),\(^10\),\(^13\) The pharmacokinetic properties do not significantly change in patients with moderate chronic liver disease or renal failure.\(^8\)-\(^10\) However, dose reductions are indicated in the elderly and in patients with diminished cardiac output due to decreased clearance of the drug.\(^14\)

EFFICACY

EGD

A randomized study of 40 patients receiving either propofol or midazolam titrated to an equivalent level of sedation prior to endoscopy reported that propofol provided more rapid recovery compared with midazolam, but was associated with pain on injection, a shorter amnesia span, and reduced patient acceptance.\(^15\) In contrast, another study randomized 90 patients to receive either midazolam or propofol administered both before and during the procedure. Patients receiving propofol tolerated endoscopy better, reached a deeper level of sedation, and recovered more rapidly. There was a similar fre-
frequency of amnesia for the procedure and perceived patient discomfort.3

Colonoscopy

An uncontrolled study of 60 patients evaluated different propofol infusion rates after a fixed loading dose during colonoscopy. Patients lost consciousness after a mean of 60.6 seconds and preservation of the hypnotic state was dependent on the infusion rate.16 A small study of 20 subjects using patient-controlled sedation (PCS) with propofol alone or in combination with alfentanil demonstrated feasibility but suggested that propofol alone did not provide adequate analgesia.17 A double-blinded study randomized 57 patients to one of three groups: diazepam/meperidine, midazolam/fentanyl, or propofol/fentanyl. There were no significant differences in sedation, analgesia, recovery rate or incidence of side-effects.18 Another randomized controlled trial compared sedation with pethidine and diazemuls versus patient-controlled sedation with propofol and alfentanil. Patient controlled sedation provided significantly lighter sedation, less analgesia, and a faster recovery time (10 vs. 40 minutes). All patients were satisfied with their level of sedation.4 Another study randomly assigned 79 patients to receive either midazolam or midazolam plus propofol. The study results are difficult to interpret due to the concomitant administration of nalbuphine and ketamine.5

ERCP

Two studies comparing midazolam to propofol during ERCP have been reported.6,7 A randomized, controlled, unblinded study of 80 patients found that adequate sedation was possible in 80% of patients with midazolam alone and 97.5% of patients receiving propofol (p<0.01). Recovery times were significantly shorter and sedation was judged by physicians and patients to be significantly better with propofol.6 In the second randomized controlled trial involving 198 patients, propofol provided more rapid sedation and significantly better patient cooperation. Recovery time was also significantly shorter with propofol (19 vs. 29 minutes).7

Combined studies

Propofol has been evaluated in three studies comprising 545 patients undergoing EGD, colonoscopy and ERCP. The authors concluded that sedation with propofol was comparable to that achieved with conventional agents, while providing for faster recovery time.2,19,20

Pediatric Use

Propofol is not approved for use in children less than 3 years of age.21 There is limited published experience on the use of propofol for endoscopic sedation in the pediatric population.22-24 A retrospective review published in abstract form reported on the successful use of propofol in 115 pediatric patients (mean age 6.4; range 10 days to 20.8 years) undergoing a variety of procedures including endoscopy in an ICU.22

SAFETY

Propofol is a respiratory depressant with effects including a reduction in minute ventilation, tidal volume, and functional residual capacity.25,26 Three studies involving a total of 300 patients receiving propofol for endoscopic sedation each reported an episode of severe respiratory depression.6,7,20 In a small study using propofol for endoscopic sedation, apnea was detected by end-tidal capnography in 6 of 10 patients. This enabled a timely decrease in the propofol infusion avoiding significant oxygen desaturation.27

The predominant cardiovascular effect of propofol is a reduction in the systemic vascular resistance, which may induce hypotension.28 When used for general anesthesia, hypotension (systolic blood pressure under 90mmHg) occurred in 15.7% and bradycardia (heart rate below 50) in 4.8% of patients.29

Infections have been reported with the use of contaminated propofol.30-32 Due to the rapid growth of organisms in this lipid based medium at room temperature, techniques to minimize contamination are critical. These include adherence to aseptic techniques, avoidance of reusing a syringe, use of propofol within 6 hours of original withdrawal from an ampule, and refrigeration.33,34

Intravenous propofol given by peripheral vein has been reported to cause pain on injection in 30-90% of patients. Reported techniques to minimize this effect include warming the drug to body temperature, dilution, use of lidocaine, or concomitant administration of select sedatives.35-40

Twenty five cases of pancreatitis associated with propofol use were reported to the food and drug administration by 1996.41 The mechanism of pancreatitis with propofol has not been established but a causality link is regarded as probable.42

COSTS

The direct cost of medication is increased with propofol compared to opioid and benzodiazepine sedation.4,26 The additional cost of monitoring and personnel for sedation has not been weighed against the shortened recovery time or other indirect patient costs.
**REFERENCES**

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